UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,884	08/31/2001	Kevin P. Baker	P2548P1C15	5993

7590 05/06/2004

BRINKS HOFER GILSON & LIONE
NBC TOWER- SUITE 3600
455 N. CITY FRONT PLAZA DRIVE
CHICAGO, IL 60611-5599

EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Advisory Action	Application No.	Applicant(s)	
	09/944,884	BAKER ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 April 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☒ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *25-29,32-34 and 38-41*.

   Claim(s) objected to: _____.

   Claim(s) rejected: *35-37,42 and 43*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation Sheet (PTOL-303) **Application No. 09/944,884**

Continuation of 2. NOTE: (i) claim 42 recites an isolated nucleic acid comprising a sequence that encodes a polypeptide of SEQ ID NO: 2 with 0-20 conservative amino acid substitution...". However, there is no support for such a limitation in the specification; (ii) the recitation of the limitaion in claim 35 "wherein said isolated nucleic acid encodes a polypeptide which stimulates release of proteoglycans from cartilage tissue" has overcome the rejection of claims 35 and 36 under 35 U.S.C. 112, 1st paragraph fo scope of enablement and written description. However, it raises a new issue in claim 37, which requires further consideration on whether the instant specification discloses any nucleic acids of 35 nucleotides in length hybridize to the nucleic acids of claim 35 and encode a polypeptide which stimulates release of proteoglycans from cartilage tissue.

Continuation of 5. does NOT place the application in condition for allowance because: the rejection of claims 35 and 37 under 35 U.S.C. 112, 2nd paragraph is maintained for the reasons set forth in the final action (page 8).

If the amendment were entered, the rejection of claims 35 and 36 under 35 U.S.C. 112, 1st paragraph, would have been overcome.

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Image AF/1646

I hereby certify that this correspondence is being deposited with the United States Postal Service, with sufficient postage, as first class mail in an envelope addressed to:
Commissioner for Patents
Alexandria, VA 22313-1450
on 12 April 2004
Date of Deposit

C. Noel Kaman, Reg. No. 51,857
Name of applicant, assignee or
Registered Representative

C. Noel Kaman
Signature

12 April 2004
Date of Signature

Our Case No. 10466-134
P2548P1C15

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Baker *et al.*

Serial No. 09/944,884

Filing Date: 8/31/2001

For SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

Examiner Ruixiang Li

Group Art Unit No. 1646

L/O Not Entered 5/14/2004 RLi

AMENDMENT AND REQUEST FOR RECONSIDERATION

Commissioner for Patents
P.O. Box 1450 - MS Non-Fee Amendment
Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action mailed February 11, 2003, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of Claims which begins on page 2 of this paper.

Remarks / Arguments begin on page 8 of this paper.

I hereby certify that this correspondence is being deposited with the United States Postal Service, with sufficient postage, as first class mail in an envelope addressed to:
Commissioner for Patents
Alexandria, VA 22313-1450
on 12 April 2004
Date of Deposit

C. Noel Kaman, Reg. No. 51,857
Name of applicant, assignee or
Registered Representative

C. Noel Kaman
Signature

12 April 2004
Date of Signature

Our Case No. 10466-134
P2548P1C15

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Baker *et al.*

Serial No. 09/944,884

Filing Date: 8/31/2001

For SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

Examiner Ruixiang Li

Group Art Unit No. 1646

AMENDMENT AND REQUEST FOR RECONSIDERATION

Commissioner for Patents
P.O. Box 1450 - MS Non-Fee Amendment
Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action mailed February 11, 2003, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of Claims which begins on page 2 of this paper.

Remarks / Arguments begin on page 8 of this paper.

This listing of Claims will replace all prior versions and listings of Claims in the application:

Listing of Claims:

Claims 1-24 (Cancelled)

Claim 25 (Previously Presented) An isolated nucleic acid encoding a polypeptide which stimulates release of proteoglycans from cartilage tissue and having at least 95% nucleic acid sequence identity to:

(a) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2);

(b) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), lacking its associated signal peptide;

(c) the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1);

(d) the full-length coding sequence of the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1); or

(e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209526.

Claim 26 (Previously Presented) The isolated nucleic acid of Claim 25 encoding a polypeptide which stimulates release of proteoglycans from cartilage tissue and having at least 99% nucleic acid sequence identity to:

(a) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2);

(b) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), lacking its associated signal peptide;

(c) the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1);

(d) the full-length coding sequence of the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1); or

(e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209526.

Claim 27 (Previously Presented) An isolated nucleic acid comprising:

(a) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2);

(b) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), lacking its associated signal peptide;

(c) the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1);

(d) the full-length coding sequence of the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1); or

(e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209526.

Claim 28 (Previously Presented) An isolated nucleic acid comprising a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2).

Claim 29 (Previously Presented) An isolated nucleic acid comprising a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), lacking its associated signal peptide.

Claims 30-31 (Cancelled)

Claim 32 (Previously Presented) An isolated nucleic acid comprising the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1).

Claim 33 (Previously Presented) An isolated nucleic acid comprising the full-length coding sequence of the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1).

Claim 34 (Previously Presented) An isolated nucleic acid comprising the full-length coding sequence of the cDNA deposited under ATCC accession number 209526.

Claim 35 (Currently Amended) An isolated nucleic acid that hybridizes under high stringency conditions to:

(a) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2);

(b) a nucleic acid sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), lacking its associated signal peptide;

(c) the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1);

(d) the full-length coding sequence of the nucleic acid sequence shown in Figure 1 (SEQ ID NO:1); or

(e) the full-length coding sequence of the cDNA deposited under ATCC accession number 209526

wherein said isolated nucleic acid encodes a polypeptide which stimulates release of proteoglycans from cartilage tissue.

Claim 36 (Currently Amended) The isolated nucleic acid of Claim 35, wherein said hybridization occurs under high stringency conditions ~~selected from the group consisting of~~ comprising:

~~(a) 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C;~~

~~(b) 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; and~~

~~(c)~~ 50% formamide, 5 x SSC (0.75 M sodium chloride, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% sodium dodecyl sulphate, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (0.75 M sodium chloride, 0.075 M sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC (0.75 M sodium chloride, 0.075 N sodium citrate) containing EDTA at 55°C.

Claim 37 (Previously Presented) The isolated nucleic acid of Claim 35 which is at least 35 nucleotides in length.

Claim 38 (Previously Presented) An isolated vector comprising the nucleic acid of Claim 25.

Claim 39 (Previously Presented) The isolated vector of Claim 38, wherein said nucleic acid is operably linked to control sequences recognized by a host cell transformed with the vector.

Claim 40 (Previously Presented) An isolated host cell comprising the vector of Claim 38.

Claim 41 (Previously Presented) The isolated host cell of Claim 40, wherein said cell is a CHO cell, an *E. coli* or a yeast cell.

Claim 42 (Currently Amended) An isolated nucleic acid comprising a sequence that encodes a polypeptide of SEQ ID NO:2 with 0-20 conservative amino acid substitutions, wherein the polypeptide stimulates release of proteoglycans from cartilage.

Claim 43 (Cancelled)

REMARKS

In the Claims:

The Examiner has indicated that claims 25-29, 32-34, and 38-41 are allowed.

Claim 35 has been amended to clarify that the claimed isolated nucleic acid which hybridizes, under high stringency conditions, to SEQ ID NO: 1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. No new matter is added by this amendment, and it is supported at pages 137-138 of the specification.

Claim 36 has been amended to clarify that the claimed high stringency conditions comprise 50% formamide, 5 x SSC (0.75 M sodium chloride, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% sodium dodecyl sulphate, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (0.75 M sodium chloride, 0.075 M sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC (0.75 M sodium chloride, 0.075 N sodium citrate) containing EDTA at 55°C. No new matter is added by the amendment, and it is supported at page 30, lines 17-21.

Claim 42 has been amended to clarify that the claimed nucleic acid has 0-20 conservative amino acid substitutions. No new matter is added by this amendment, and it is supported at page 61 of the specification.

Claim 43 is cancelled herein without prejudice or disclaimer.

Rejections Withdrawn:

Applicants thank the Examiner for withdrawing the rejection of claims 25-29, 32-34, and 38-41 under 35 U.S.C. § 112, first paragraph for scope of enablement; for withdrawing

rejection of claims 25-29, 32-34, and 38-41 under 35 U.S.C. § 112, first paragraph for written description; for withdrawing rejection of claims 25-27, 36, and 38-41 under 35 U.S.C. § 112, second paragraph for indefiniteness; for withdrawing rejection of claim 37 under 35 U.S.C. § 102(b) as being anticipated by Dreher *et al;* and for withdrawing the objection to claims 28, 29, and 32-34.

Request for Reconsideration:

Claim Rejections under 35 U.S.C. § 112, first paragraph:
Enablement:

The Examiner has maintained rejection of claims 35-37 under 35 U.S.C. § 112, first paragraph, alleging that one skilled in the art would be forced into undue experimentation to practice the invention as broadly as it is claimed. Specifically the Examiner contends that the claims are remarkably broad and encompass a genus of nucleic acids that vary substantially both in length and in nucleotide composition. As an example, the Examiner argues that the specification fails to teach an artisan how to use the variants of the nucleic acid encoding SEQ ID NO:2 that do no possess the same activity as that of the nucleic acid encoding the amino acid of SEQ ID NO:2.

Applicants have amended claim 35 such that any claimed nucleic acid that hybridizes to SEQ ID NO:1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 must encode a polypeptide that stimulates release of proteoglycans from cartilage tissue. Thus, one of skill in the art would know how to use variants of SEQ ID NO:2 that hybridize under high stringency conditions. Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

The Examiner rejected claim 42 for overbreadth, noting that the claim scope encompasses a sequence where every amino acid of SEQ ID NO:2 is substituted. The Examiner kindly noted that an acceptable percent amino acid/or nucleic acid sequence identity is required to overcome the rejection of claim 42. Per the Examiner's kind

suggestion, claim 42 has been amended to encompass a sequence with only 0-20 conservative amino acid substitutions. SEQ ID NO: 2 is 379 amino acids long. Thus, an amino acid sequence with 20 conservative amino acid substitutions would have 94.7% sequence identity to SEQ ID NO:2. This is an acceptable percent amino acid/nucleic acid sequence identity and therefore, Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

Written Description:

The Examiner has maintained rejection of claims 35-37 under 35 U.S.C. § 112, first paragraph for lack of written description. The Examiner contends that the claims encompass "an enormous genus of nucleic acids that vary substantially both in length and in nucleotide composition." Specifically, the Examiner argues that the claims do not require that the nucleic acid possesses any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature."
Applicants have amended claim 35 to clarify that the claimed isolated nucleic acid which hybridizes, under high stringency conditions, to SEQ ID NO: 1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. Thus, the amended claims require that the hybridizing nucleic acid not only hybridize under high stringency conditions and encode a polypeptide that stimulate release of proteoglycans, but also allow one of skill in the art to distinguish nucleic acids within the scope of the claimed genus from those falling outside the scope of the claimed genus.

The Examiner further argues that the specification fails to provide a reasonable number of representative species of the claimed genus. Applicants respectfully disagree.

The analysis for determining whether the present specification provides written description support for the invention defined by claims 35-37 may be performed by numerous methods, several of which are described in the Guidelines and further exemplified in the Revised Interim Written Description Guidelines Training Materials ("Written Description Training Materials"), published on the USPTO website at

http://www.uspto.gov/web/offices/pac/writtendesc.pdf. These Written Description Training Materials provide additional clarity to the Guidelines published in the Federal Register, Volume 66, No. 4, pages 1099-1111.

With regard to claims 35-37, the present situation is analogous to Example 9 found at pages 35-37 of the Written Description Training Materials. More specifically, in Example 9 on pages 35-37 of the enclosed Written Description Training Materials, a claim directed to "[a]n isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO:1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity" is analyzed for compliance with the written description requirement. In this example, the essential feature of the claimed invention is the isolated nucleic acid that hybridizes to SEQ ID NO:1 under highly stringent conditions and encodes a protein with a specific function. There is a single species disclosed (a molecule consisting of SEQ ID NO:1) that is within the scope of the claimed genus. Finally, the art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions was conventional in the art at the time of filing. The Written Description Training Materials conclude that the above claim is supported by an adequate written description because "a person of ordinary skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs." The Written Description Training Materials also conclude that disclosure of a single cDNA sequence in this context is a sufficient representative number of species.

All of the just-mentioned requirements are met by this application as well as the currently pending claims. In particular, the essential feature of amended Claims 35-37 is an isolated nucleic acid that hybridizes to SEQ ID NO:1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2, and which also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. There is a species (SEQ ID NO:1) disclosed within the scope of the claims and high stringency

conditions were both well known in the art as of the filing date of the present application and are defined at page 30 of the specification.

Given the abovementioned factors, Applicants respectfully submit that Claims 35-37 satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, and therefore, respectfully request that this ground of rejection be withdrawn.

The Examiner also rejects claim 42 under 35 U.S.C. § 112, first paragraph for lack of written description alleging that due to the breadth of the claimed genus and the lack of the definitive structural features of the genus, one skilled in the art would not recognize from the disclosure that Applicants were in possession of the claimed genus.

Applicants respectfully disagree. Applicants have amended claim 42 to encompass a sequence with only 0-20 conservative amino acid substitutions. As discussed above, SEQ ID NO: 2 is 379 amino acids long and therefore, an amino acid sequence with 20 conservative amino acid substitutions would have 94.7% sequence identity to SEQ ID NO:2. Thus, amended claim 42 is not overly broad. Further, one of ordinary skill in the art would recognize from the required functional identity and sequence identity that Applicants had possession of this claimed genus at the time of filing. Hence, Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

New Matter:

Applicants have cancelled claim 43 herein without prejudice or disclaimer and therefore respectfully request that this ground of rejection be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 35 and 37 as being indefinite. The Examiner alleges that claim 35 is indefinite because it recites "under high stringency conditions," without defining the hybridization conditions in the claims. The Examiner contends that neither the art, nor the specification, provides an unambiguous definition of what qualifies as "high stringency conditions."

Applicants respectfully disagree. At page 30, lines 12-21 of the specification, Applicants specifically define "high stringency conditions" as:

> . . . those that: (1) employ low iconic strength and high temperature for washing, for example 0.015M sodium chloride / 0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate, 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml, 0.1% SDS, and 10% dextran sulfate at 42 °C, with washes at 42 °C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55 °C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55 °C.

Applicants note that they have previously directed the Examiner's attention to the above definition found on page 30 of the specification. In response, the Examiner argued that the definition only provides exemplary conditions and pointed to the use of "for example" on page 30.

Applicants respectfully disagree. The definition of "high stringency" found on page 30 of the specification from line 12-21 only uses the phrase "for example" to refer to one example of a denaturing agent that might be used. Other than that example, the definition of "high stringency conditions" found on page 30 is not exemplary and use of the phrase "as defined herein," indicates that Applicants intended to set forth a definition of "high stringency conditions."

Further, Applicants disclose that additional detail and explanation of stringency of hybridization reaction may be found at Ausubel et al., *Current Protocols in Molecular Biology*, Wiley Interscience Publishers (1995). Thus "high stringency conditions" as used in claims 35 and 37 is not indefinite.

Applicants have overcome this ground of rejection and respectfully request that the Examiner reconsider and withdrawn this rejection of claims 35 and 37.

Claim Rejections Under 35 U.S.C. § 102(b):

The Examiner has maintained rejection of claims 35 and 36 under 35 U.S.C. § 102(b) as being anticipated by Dreher *et al.* Applicants have amended claim 35 to clarify that the claimed isolated nucleic acid which hybridizes, under high stringency conditions, to SEQ ID NO: 1 or to the nucleic acid encoding the polypeptide of SEQ ID NO:2 also has the property of encoding a polypeptide that stimulates release of proteoglycans from cartilage tissue. Dreher *et al.* does not teach that the disclosed nucleic acid sequence encodes a polypeptide that stimulates release of proteoglycans from cartilage tissue. Hence, claims 35 and 36 are not anticipated by Dreher *et al.*, because according to the MPEP § 2131, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Thus, Applicants have overcome this ground of rejection and respectfully request that it be withdrawn.

Conclusion

The Examiner has allowed claims 25-29, 32-34, and 38-41. Applicants believe that currently pending Claims 35-37 and 42 are also allowable. Hence, Applicants respectfully request that the Examiner grant allowance of this application. The Examiner is invited to contact the undersigned attorney for Applicants via telephone if such communication would expedite the prosecution this application.

Respectfully submitted,

C. Noel Kaman

C. Noel Kaman
Registration No. 51,857
Attorney for Applicant

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4200